A single-blind prospective Randomised Control Trial (RCT) to investigate the need for a transition phase following successful completion of functional appliance therapy and a sample size calculation pilot study

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Joanna Thomson

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Structured Abstract

Aims

The aim of this study was to investigate whether transition following successful completion of functional appliance therapy was important in retention of the corrected overjet.

Objectives

The main objective was to investigate whether a transition phase following successful completion of functional appliance therapy was important in retention of the corrected overjet.

In addition, a secondary objective was to perform a pilot study to aid in a sample size calculation for a larger trial to investigate the effect of transition versus no transition following successful completion of functional appliance therapy.

Null Hypothesis

There is no difference in the effect of a transition phase versus no transition on the corrected overjet following successful completion of functional appliance therapy.

Design

A single-blind prospective pilot Randomised Control Trial (RCT) to investigate the need for a transition phase following successful completion of functional appliance therapy.

Ethical Approval

Ethical approval was sought and obtained from the National Research Ethics service (NRES) and the NHS Research and Development Offices. This study was given the REC reference number: 12/NW/0565.

It was necessary to gain to ethical approval as this was a research project. That meant that it must be approved by a formal research ethic committee. In general there is a grey area between audit

and research and the distinction is difficult to agree on. This project was thought of as research instead of an audit of effectiveness as there was no clinical guidelines or gold standards to make a comparison too and therefore less like an audit. The groups were also randomised for differing treatment options for patients who were in similar clinical situations and in that case ethical approval should be sought.

Setting

Patients attending for treatment at the Orthodontic department of the Liverpool University Dental and Arrowe Park Hospitals.

Sample Size

As this was a pilot study, no sample size calculation had been carried out. The target sample size was set at 30, to allow estimation of outcome proportions.

Participant selection

Inclusion criteria

- The subjects entered into the trial would have completed Clark's Twin Block (CTB) phase of treatment and require fixed appliance treatment.

Exclusion criteria

- Patients who do not progress into fixed appliance therapy due to low treatment need (clinician decision) or low patient interest (patient decision).
- Patients included in the trial but drop out for any reason, would be included in the statistical intention-to-treat analysis (bias reduction).
- Patients with craniofacial syndromes or clefts of the lip and/or palate.

Randomisation

The randomisation process allocated subjects to the transition or no transition groups. The randomisation sequence was generated by a statistician by use of a computer program. The statistician was blinded to the recruitment process. The groups were then stratified by the Orthodontic Consultant. The treatment allocation was typed onto a card and placed in sequentially numbered opaque envelopes. These were kept in the Orthodontic Department along with a log of envelope allocation.

Interventions

Group A- transition group (standard care)

Patients undergoing transition by any clinically-based method that was indicated for a period up to three months.

Group B- no transition group (intervention)

Patients were bonded up with fixed appliances as soon as the CTB phase of treatment was been completed. Class 2 mechanics were not immediately applied in the intervention group. This followed normal treatment protocol.

Blinding

Patients- Aware that they were receiving treatment to correct their malocclusion (not blinded)

Clinicians- Aware of whether or not a transition phase was being used to maintain the overjet correction (not blinded)

Assessors- Unaware measurements carried out clinically (blinded)

Method

Patients were randomly allocated to either Group A (Standard care) or Group B (intervention). They were then followed up monthly for a period of three months. At each monthly visit, clinical measurements of overjet were taken. At the end of this period the clinical measurements were analysed by a blinded assessor who was unaware of the allocation of the treatment.

Outcome measures

The primary outcome variable was the presence/absence of a corrected overjet at the end of the study within 2mm of the overjet at the end of Twin Block therapy.

The overjet measurements were based on clinical findings.

Statistical analysis

Data was transferred from the data collection forms on a Microsoft© Excel spreadsheet and SPSS© software was used for the statistical analysis.

As a pilot, efficacy testing was not one of the primary aims of this study, as the study was not powered to detect a difference. However, a statistical analysis of the primary outcome data was be carried out, using Fisher's exact test to compare the proportions with retention of the corrected overjet at the end of the trial.

The primary outcome was retention of the corrected overjet.

Results

- The recruited sample was primarily female at 66.6% compared to males at 33.3%. Females were shown to have a higher success rate than males at 80%; however these results were not significant.
- The average overjet in Group A was 7.1 mm. The average overjet of the successful patients in Group A was 7.3 mm and 7 mm in the unsuccessful patients.
- The average overjet in Group B was 10.5 mm. The average overjet in the successful patients in Group B was 11.3 mm and 9.3 mm in the unsuccessful patients.
- In Group A, 1 successful and 1 unsuccessful patient attended the casuals' clinic. In Group B, 3 successful and 1 unsuccessful patients attended the casuals' clinic.
- In the total sample only 1 patient cancelled an appointment, this appointment was subsequently rearranged for within 2 weeks of original date.
- In the total sample only 1 patient failed to attend an appointment.
- All patients in the study had a Dental Health Component (DHC) of either a 4a or 5a. 33.3% had a DHC component of a 5a and 66.66% had a 4a.
- A Fisher's exact test was carried out to compare the proportions with retention of the corrected overjet. The *p* value was 0.643 (Appendix 1) which was substantially higher than the 0.05 level of statistical significance set for this study.

Conclusion

1. The null hypothesis could not be rejected based on the results of this study. Therefore, there is no evidence of difference in using any form of transition following successful completion of functional appliance therapy compared to no transition.
2. A secondary objective of this study was to investigate the size of sample size needed to appropriately power a project of this type. This was measured to 97 patients per group with α set at 80% and significance level of 0.05.
3. Due to the small sample size, the study was not powered to detect a clinical significance difference between the groups and therefore it is not possible to determine if the intervention is better at maintaining the control group than the standard care group
4. This pilot did not give sufficient information to accurately estimate the proportion of successful retention of the overjet in the transition group.
5. The investigation was not continued after the doctoral project was complete due to problems with recruitment and lack of personnel to continue the study.

Table of Contents

1.0 Literature Review

1.1 Introduction

Functional appliance therapy is the mainstay of orthodontic treatment aimed at the reduction of an increased overjet often found in association with Class II malocclusion in the growing patient. It has long been debated whether there is a need for a transition period following the use of functional appliances or if progression into the fixed appliance phase can be implemented without a relapse of the corrected overjet in the treatment of Class II malocclusion. The most popular functional appliance in use in the United Kingdom (UK) today is the modified Clark's Twin Block (CTB) (Clark, 1988).

The need for appliance transition following an active phase of functional appliance therapy has become evident in certain instances where a return of the original malocclusion features has been observed. The most prominent aspect of those features has been an increased overjet. This, in turn, could potentially lead to a need for tooth extraction in the maxillary arch to re-establish the corrected overjet. There are a number of methods commonly used in clinical orthodontics to carry out the transition phase (Fleming *et al*., 2007). These may range from nocturnal appliance wear, trimming of the occlusal surfaces of the lower blocks to facilitate closure of lateral open bites, construction of an Upper Removable Appliance (URA) with a steep incline bite plane or immediate progression into fixed orthodontic appliances with early use of inter-maxillary traction (Class II traction). The alternative would be the cessation of the functional appliance wear in order to evaluate the potential relapse prior to fixed appliance treatment progression.

Elimination of the transition phase could precipitate into several advantages. Primarily, it would reduce treatment time by approximately three months, with obvious implications in reduction of

clinical time and treatment cost. In addition, there have been suggestions in the literature that shorter treatment duration is associated with improved patient compliance with treatment (Royko *et al*., 1999). The focus of functional appliance treatment in the literature has been predominantly concerned with the mode of action of functional appliances (Dermaut & Aelbers, 1996). On the other hand there is a paucity of evidence regarding the appropriateness of the transition stage. This research could potentially fill in a void in the understanding of a mode of treatment that is in use by orthodontist worldwide.

1.2 History of functional appliance treatment

One of the earliest designs of a type of functional appliance was by Norman Kingsley, who created an upper removable appliance with the following components;

1. molar clips
2. continuous labial wire
3. posterior bite blocks

The proposed use of this appliance was to posture the mandible forward. Wahl (1996) reviewed the history of functional appliances quoting Norman Kingsley (1879) 'The object was not to protrude the lower teeth, but to change or jump the bite in case of an excessively retreating lower jaw'. This could be considered to be the forefather of modern day functional appliances. In the United States of America (USA), Edward Angle (1907) used a fixed type of functional appliance with interlocking rings on first molar bands to posture the mandible forward.

Pierre Robin (1902) was another pioneer of functional appliances. His proposed design supposedly stretched the facial muscles by altering the sagittal relationship of the maxilla to the mandible. This monobloc appliance was an adaption of Kingsley's maxillary plate (Kingsley, 1880).

The appliance extended across the lingual surfaces of the mandibular teeth as well as lingual indentations of both maxillary and mandibular teeth. Furthermore, it incorporated an expansion screw to allow transverse expansion of the maxillary arch. The original purpose of this appliance was to suit children with glossoptosis syndrome recently re-named Pierre Robin syndrome. The appliance acted as a passive positioning device for patients with a micrognathic mandible and posterior position of the tongue, which could potentially obstruct the airway.

This idea was further developed by Viggo Andresen in (1909), who designed the Activator, which was a tooth-borne, loose fitting passive appliance. The original design featured facets that directed erupting posterior teeth mesially (mandible) or distally (maxilla). He proposed the appliance had a loose fit in the mouth and therefore it transferred the stimuli from the teeth to the supporting muscular structures. It was a controversial appliance which was further developed and refined and eventually became an extremely popular appliance in Europe.

Another early user of functional appliances was Emil Herbst (1905) coining the synonymous appliance. This was a fixed functional design and thought suitable for older children who, potentially, could not tolerate a removable appliance. The appliance consisted of a telescopic arm that was attached to the maxillary first molars and a cantilever connection attached to the mandibular first molars. This appliance was not widely used until Hans Pancherz revived interest for it in the 1970's (Pancherz, 1979).

In 1956, Martin Schwartz attempted a combination of the activator and the active plate by constructing separate mandibular and maxillary components that were designed to posture the mandible forward. This appliance echoed the design of half a century earlier by Pierre Robin.

Another appliance was the Bionator designed by Wilhelm Balters (Balters 1964, 1969) which was

a modification of the Andreessen Activator.

In 1966 Rolf Frankel, created an appliance that was entirely mucosa borne. He proposed that the corrected malocclusion will remain stable if the structural and functional deviations of the muscular system are corrected. He created three appliances, the Functional Regulator I, II and III for treating Class I, Class II and Class III malocclusions respectively (Frankel, 1966). This was received well in the USA eventually becoming a popular appliance at that time.

In 1977, William Clark designed the modern day functional appliance that became the Twin Block (Clark, 1988). It is presently the most commonly used functional appliance in the UK. The CTB is a development of Pierre Robin's monobloc and Schwarz's double plate. It consisted of upper and lower bite blocks interlocking at an angle of 45°. The bite blocks were set at 5-6 mm thick in the premolar region with 1-2 mm in the molar region in order to allow eruption of the lower molar segments. The original design incorporated the use of a Concorde facial bow for extra oral traction as this was thought to be of use in high angle patients.

1.3 The use of functional appliances in contemporary Orthodontic treatment

The most popular functional appliance in use in the UK today is the modified CTB (Chadwick *et al*., 1998). The CTB appliance achieves its effects through forces arising from the masticatory and facial muscles (Fleming *et al*., 2007; Ghafari *et al*., 1998). It is commonly used to treat Class II or in certain instances Class III malocclusions (Seehra *et al*., 2010). Functional appliances are often used in the younger age groups during the growth spurt. The other clinical indications for a functional appliance include anchorage demanding crowded Class II cases. They can also be used as an early intervention appliance in the mixed dentition as well or a compliance 'tester'. Lastly it can also be used in the instances that oral hygiene is not at the standard required for fixed

appliance treatment.

1.4 Mode of action of functional treatment

There has been a significant amount of controversy regarding the mode of action of functional appliances. Some workers have claimed that skeletal growth of the mandible was feasible. These claims were scientifically unsubstantiated and remain largely unproven. Another body of evidence has suggested that the mode of action is mostly dento-alveolar (O'Brien *et al*.; 2003, Ghafari *et al*.; 1998, Keeling *et al*.; 1998, Tulloch *et al*.; 1997).

The body of evidence is divided into animal laboratory studies and human RCTs or well controlled cephalometric based studies.

1.4.1 Animal studies

Woodside (1987) using cappucian monkeys experimented with the Herbst appliance. The results of this study showed the mandible did move forward into a more anterior position. The study also showed that an element of normal growth was present, attributing some of the correction seen. Furthermore there was extensive glenoid fossa remodelling on the treated subjects. This study however suffered from lack of adequate controls.

Studies carried out by Woodside (1987) on rats suggested that functional appliances cause lateral pterygoid muscle stretching, stimulation of growth factors and promoting condylar growth. There was also a suggestion of remodelling of the glenoid fossa.

Dermaut and Aelbers (1996) carried out a study using various animal models. Their study showed cartilage proliferation in the pre-chondroblastic zone. It suggested an increase in the effective length of the mandible and remodelling of the glenoid fossa as well as maxillary restraint with extra oral traction. Similarly, glenoid fossa remodelling was a common finding. The limitations of

study were a small sample size and an artificially introduced skeletal discrepancy.

The Petrovic *et al* (1979) study suggested that anterior posturing of the mandible in growing rats can precipitate additional growth of the condylar cartilage causing an increase in mandibular growth by stimulating the cells in the proliferation zone. Another study by Tsolakis *et al* (1997) reported an increase in the mandibular length.

More recently Rabie *et al* (2003) investigated an alteration of gene expression in rats that had been treated with a functional appliance. This study showed that a transcription factor, SOX-9, that targeted type II collagen, was up regulated in the glenoid fossa following mandibular posturing. This also induced cell signalling molecules in the proliferation zone of the cartilage. All of these findings have been interpreted as evidence that functional appliances enhance condylar growth. This was only a transient effect as no long term follow up was carried out.

The evidence in the literature has shown that posturing of the mandible in animal models can cause an alteration in the surface contours of the condyle, glenoid fossa and posterior glenoid tubercle. Furthermore, condylar growth can be directed in a more posterior direction as well as stimulate growth factors and alter gene expression. However, the results cannot be extrapolated to human treatment easily. The main problems with this type of research were:

1. Small sample size
2. Poor long term follow up
3. No element of compliance
4. Artificially induced malocclusions

In contrast there has been an extensive body of evidence regarding human research that perhaps is more applicable to clinical orthodontics.

1.4.2 Human studies

There have been a number of clinical Trials carried out investigating the effect of functional mandibular growth. In general they all have shown small differences in the mandibular length of the passive tooth borne appliances.

Ruf and Pancherz (1998) carried out a study to investigate the effect of the Herbst appliance on the glenoid fossa and the condyle. They used Magnetic Resonance Imaging (MRI) was used to assess the TMJ anatomy. The results showed condyle and glenoid fossa remodelling.

Dermaut and Aelbers (1996) in their review of the literature had stated a number of findings,

1. Different response of males and females to treatment
2. Inhibition of maxillary growth was seen in 33% of activator or Herbst studies
3. Mandibular growth was affected in 68% of Herbst and Activator studies
4. The Herbst appliance showed a mean reduction in ANB of 3.5 and increased mandibular length (Co-Gn) of 4 mm.
5. Maxillary length changes never exceeded 1 mm
6. Negligible changes in palatal plane

This study highlighted that with the Herbst appliance by Ruf and Pancherz (1998) lacked long term follow up to substantiate the proposed long term effects of the appliance.

Another study by Sandler and Lund (1998) further reinforces that the effects of the functional appliance were dento-alveolar rather than skeletal. The study reported statistically significant results in relation to the following

1. Reduction of ANB of 2
2. Increase in SNB of 1.9

3. Increase of Ar-Pog compared to control
4. Maxillary incisor retroclination of 10.8°
5. Mandibular incisor proclination of 7.9°

They concluded that the overjet was reduced by the forward movement of the mandible. The buccal segments were corrected by lower molar eruption and the restraint of maxillary molars eruption. They also concluded that the main contributing factor in reducing the overjet was the effect that the appliance had on the dento-alveolar structures.

Chen *et al* (2002) carried out an analysis of the efficacy of functional appliances on mandibular growth. This was a meta-analysis concluding that there was no evidence to suggest a change in the mandibular length.

In conclusion, the current concepts that are widely accepted for the mode of action of functional appliances are;

1. Dento-alveolar changes causing the maxillary teeth to move more posteriorly and the mandibular teeth anteriorly
2. A restriction of the maxillary growth
3. Very little evidence of permanent mandibular growth
4. Glenoid fossa remodelling causing forward positioning of the condyle

As with animal studies, human studies also have their drawbacks, this is because a large number of the human studies have used cephalometric measurements taken from lateral cephalogram radiographs, where a chance of error in measurements exists (Baumrind and Frantz, 1971). The control groups can be difficult to match as it is unethical to withhold treatment if deemed clinically necessary. Overall, as with most dental/orthodontic studies they suffer from a small

sample size.

1.5 Timing of functional appliance treatment

As with all areas of research related to functional appliance treatment, treatment timing has been another controversial field. There is various different treatment approaches centred round one or two phase treatment plans. One of the common ways to treat the Class II malocclusion involves a functional appliance at age range 7-10 years old. At the conclusion of the first phase of treatment fixed appliances would be utilised. The delay would be due to the anticipation of the establishment of the permanent dentition. This method of treatment potentially is limiting since the patients experience a longer course of treatment. Another limiting factor may be a longer period of retention in order to maintain the corrected overjet. The alternative would be to provide a single or one phase course of treatment. Conversely this is achieved by progressing to fixed appliances at the conclusion of the functional appliance treatment.

The available scientific evidence from RCT's in the USA and United Kingdom (UK), have attempted to shed light on treatment timing.

Table 1 illustrates the main findings of studies on functional appliances.

Authors	**Year**	**Appliance**	**Summary of results**
Tulloch *et al*	1997	Bionator appliance and extra oral traction	Variation of growth whether or not treatment was carried out (31% controls had favourable growth improvements) Early treatment group had initial skeletal change but and end of phase 2 of treatment no difference when compared to the late treatment group No difference in PAR score between early and late treatment scores Early treatment group in fixed appliance for shorter time (only approached significant) Percentage going onto surgery similar Percentage having extractions not significant but approached significance for early treatment having more extractions
Keeling *et al*	1998	Bionator appliance and extra oral traction with URA with bite plane	Extra oral traction and Bionator do not affect maxillary growth in 9-10 year old patients Both appliances enhance mandibular growth Skeletal changes achieved are stable No difference between early and late treatment

			groups at end of phase two
Ghafari *et al*	1998	Frankel appliance and extra oral traction	Both effective at treating Class II division 1 malocclusions Timing not critical leave till late childhood Extra oral traction greater effect on the molars Frankel had greater overjet reduction Compliance poor with the appliance

Fig 1. Landmark studies on the mode of action of functional appliances with a summary of the main results.

Since the O'Brien (2003) study was conducted in the United Kingdom (UK), it has been suggested that it is most relative to treatment provided in the UK. The second part of the study related the physical effect to the psychosocial influence of treatment. They concluded that the overjet reduction was due to dento-alveolar effects with minimal influence to the skeletal bases. The second part of the study found that treating patients at a younger age could improve self-concept with less negative social experiences.

1.6 The modified Clark's Twin Block

In 1977, William Clark designed functional appliance that is the Twin Block (Clark, 1988). Its modification has become the most commonly used functional appliance in the UK (Chadwick *et al*., 1998). The modified CTB that is currently used consists of upper and lower bite blocks which interlock at an angle of 45°. He originally suggested that the bite blocks were to be of 5-6 mm thick in the pre molar region and 1-2 mm in the molar region to allow eruption of the molar segments. Retention was provided by modified double arrowhead clasps that usually spanned

two buccal teeth and with a tube soldered onto the clasp for the attachment of extra-oral traction. The other features of the upper appliance included a midline expansion screw and a labial bow that extended from one upper first permanent molar to the other. The lower appliance was retained in the permanent dentition by inter-dental clasps in the incisor and premolar region. A reverse 'U' loop was placed lingually to the lower central incisors to allow the attachment of inter-maxillary traction. It was also stated that the bite blocks should only cover the palatal cusps of the upper maxillary cusps to improve retention. A Concorde face bow was to be worn simultaneously with the appliance. The Concorde face bow had similar design features to other forms of extra oral traction with the addition of a midline labial hook to allow the use of inter maxillary traction. There have been several modifications by the author ever since. In the lower appliance, the reverse 'U' loop and inter- dental clasps in the premolar region were removed and replaced by ball ended clasps for retention in the incisor region. For retention in the premolar region delta clasps were introduced.

The designs that currently are in use stem from this original design. The upper appliance uses Adams cribs for retention and a labial bow. The Concorde bow is not usually used. In the lower arch the Delta clasps have been replaced by Adams clasps.

1.7 Transition phase- Progression into fixed orthodontic appliances

Current literature contains limited number of articles relating to the transition from functional appliance to fixed appliance treatment. A clinical overview was written by Fleming, Scott and DiBiase (2007) on how to manage the transition phase. They suggested that correction must be maintained during the aligning and levelling stages until stainless steel arch wires and Class II traction can be utilised. The relapse in the transition stage could be postural with repositioning

of the mandibular condyle and uprighting of the distally tipped maxillary dentition. The key in preventing relapse is appropriate management of these factors in the transition stage and early phases of fixed appliance treatment. The paper suggested that overcorrection of the overjet resulting in an edge to edge or Class III incisor relationship and molar relationship could be desirable.

Extra oral traction could be advantageous in maintenance of the overjet correction and molar relationship and it allows the clinician to proceed directly into fixed appliances. Lastly extra oral traction could be introduced on the withdrawal of the functional appliance and worn during the aligning and levelling stages and can be withdrawn when in a stainless steel archwire. The biggest disadvantage in using extra oral traction would be the reduction of compliance of the patient.

Another method of transition is nocturnal use of the appliance. Some clinicians prefer the patient to wear the appliance at night-time only as it is thought to maintain the neuromusculatory response and remodelling effects of the condyle (Fleming *et al*., 1997). It is thought to help maintain the overjet correction and molar relationship and the appliance could be modified to allow fixed appliances to be placed at the same time.

Another method of maintain the correction is with an appliance termed 'Steep and Deep' (Sandler and DiBiase, 1996). This is a removable appliance with an inclined bite plane that is worn continuously and can also be altered to be used concurrently with fixed appliances. A bite plane of at least 8 mm deep and at an inclination of 70 degrees to the horizontal has been described (Sandler and DiBiase, 1996). This appliance is useful as it allows the closure of lateral open bite whilst still maintaining the Class II effect. The use of the steep and deep appliance has its limitations as it can cause proclination of the lower labial segment and it has to be of sufficient

depth to allow occlusion anterior to the bite plane to prohibit a relapse in the corrected overjet. In theory it could cause differential eruption of the second molars resulting in increased vertical dimension in high angle cases.

Another method would be progression into fixed appliance with early use of Class II inter maxillary traction (Fleming *et al*., 1997). The disadvantage of inter maxillary elastics is that it could potentially further procline the lower incisors as well as downward and backward rotate the mandible and lingually tip the lower molars.

1.8 Conclusion

There is a trend amongst all the literature of an air of uncertainty to the mode of action of these appliances with contrasting opinions and scientific evidence. It is clear that there is still a potential to learn more in this area and hopefully the future will bring definitive answers to the questions that we pose. It is hoped that this research study will bring about some concrete evidence that will be a starter point for further investigations.

1.9 Rationale for research

After searching through the literature in this area, it was apparent that there was a paucity of research into the transitional stage of twin-block appliance therapy. There is no evidence to base a clinical decision on when to proceed to the transition stage or if this stage is even necessary. There have never been any clinical Trials investigating if this area and this is why that I have decided on this area for research.

2.0 Study: Aims and Objectives

2.1 Aims

The aim of this study was to investigate whether transition following successful completion of functional appliance therapy was important in retention of the corrected overjet.

2.2 Objectives

The main objective was to investigate whether a transition phase following successful completion of functional appliance therapy is important in retention of the corrected overjet.

In addition, a secondary objective was to perform a pilot study to aid in a sample size calculation for a larger trial to investigate the effect of transition versus no transition following successful completion of functional appliance therapy.

3.0 Null Hypothesis

There is no difference in the effect of transition versus no transition following successful completion of the functional appliance therapy on the corrected overjet.

4.0 Materials and Methods

4.1 Ethical approval

Ethical approval was sought and obtained from the National Research Ethics service (NRES) and the NHS Research and Development Offices. This study was given the REC reference number: 12/NW/0565.

4.2 Study Design

4.2.1 Inclusion criteria

- The subjects entered into the trial would have completed Clark's Twin Block (CTB) phase of treatment and require fixed appliance treatment.

4.2.2 Exclusion criteria

- Patients who do not progress into fixed appliance therapy due to low treatment need (clinician decision) or low patient interest (patient decision).
- Patients included in the trial but drop out for any reason, would be included in the statistical intention-to-treat analysis (bias reduction).
- Patients with craniofacial syndromes or clefts of the lip and/or palate.

4.3 Recruitment

Patients were invited to participate if they fulfilled the inclusion criteria. They were recruited from patients attending for treatment at the Orthodontic department of the Liverpool University Dental and Arrowe Park Hospitals.

4.4 Randomisation

The randomisation process allocated subjects to the transition or no transition groups. The randomisation sequence was generated by a statistician by use of a computer program. The statistician was blinded to the recruitment process. The groups were then stratified by the Orthodontic Consultant. The treatment allocation was typed onto a card and placed in sequentially numbered opaque envelopes. These were kept in the Orthodontic department along with a log of envelope allocation.

4.5 Blinding

Patients- Aware that they were receiving treatment to correct their malocclusion (not blinded).

Clinicians- Aware whether or not a transition phase is being used to maintain the overjet correction (not blinded).

Assessors- Unaware measurements carried out clinically (blinded).

4.6 Consent

Written informed consent was obtained from the parents of the children who participated in the study and for the intended treatment. A separate written consent was obtained from the patients (Appendix 10.1 and 10.2).

At the first appointment, all eligible patients and their parents had the study explained to them verbally and were invited to ask any questions that may have arisen. They were given all the relevant patient information leaflets. The patient was then given a review appointment.

At the second appointment, another opportunity was given for the patients to ask any questions that the patient information leaflet brought to light. They then confirmed their participation in the study. Written informed consent was obtained from all the patients entered into the trial.

4.7 Sample size

As this was a pilot study, no sample size calculation had been carried out. The target sample size was set at 30, to allow estimation of outcome proportions.

4.8 Treatment

Treatment was carried out by post-graduate students in Orthodontics at the Orthodontic Departments of the Liverpool University Dental Hospital and Arrowe Park Hospital. An official brief on the study and the protocol for the accepted patients was circulated to clinical and nursing staff.

Patients fulfilling the inclusion criteria were invited to participate.

Group A- transition group (standard care)

Patients underwent transition by any clinically-based method that was indicated for a period up to three months.

Group B- no transition group (intervention)

Patients were bonded up with fixed appliances as soon as the functional phase of treatment was been completed.

4.9 Protocol Deviation

At any point the patient was free to withdraw their consent.

There was a standard departmental wide protocol for patients who Failed To Attend (FTA).

1st FTA - another appointment was sent out in the post and logged into the notes.

2nd FTA- a letter was sent out asking the patient to contact the department to make another appointment. If there is no contact within 2 weeks then a phone call to the patient was made.

3rd FTA- Patient was contacted directly by phone asking them to come into the department. They were asked if they wished to continue treatment and emphasised the importance of keeping their appointments.

4.10 Unable to Attend (UTA) protocol

Patients were to be contacted to make another appointment by either telephone or by sending a new appointment out to them.

4.11 Casualty protocol

Patients were given information to contact the department if any breakages/problems arose with the treatment. It will not be possible for a single operator to treat all the patients that present with breakages during the trial due to the number of patients involved. However the department's casual protocols were followed.

4.12 Breakages protocol

In the event of a breakage, the patient would be seen at the same day. If the circumstances did not permit this, it would be endeavoured to see the patients as soon as possible.

4.13 Patients who fail to complete the trial

If any patients withdraw their consent then it may not be possible to include them in the final statistical analysis.

4.14 Assessment of patient response

The primary outcome variable was the presence/absence of a corrected overjet at the end of the trial within 2 mm of the overjet at the end of Twin Block therapy. The overjet measurements were based on clinical findings.

4.15 Data collection

Baseline data for both treatment groups included the following:

Clinical measurements: Overjet, overbite, molar relationship, canine relationship and dental centrelines.

Data collected on the patient's medical, social and dental history, their skeletal pattern, dental health, occlusal and TMJ status. This data were stored as linked anonymised data.

In addition, the number of failed appointments, cancelled appointments, number of visits to the casual's clinic and the total overall number of appointments were recorded.

The Index of Orthodontic Treatment Need (IOTN) was calculated on the Angle-trimmed study plaster models.

The trial started when the patient was deemed ready to proceed into the transition stage. This was when the patient had an overjet of between 0 and 4 mm.

- Data collection point 1 (start point) – at end of Twin Block therapy: Clinical measurements
- Data collection point 2 (end point) – following three months: Clinical measurements

4.16 Data storage

Data were entered on specifically designed data collection forms in addition to being entered into the patients' medical notes .The forms were in the medical notes and removed when collating the data into a secure filing cabinet.

The model boxes were stored as per normal departmental protocol within a secure area within the department.

The radiographs were stored in the patients' cases notes in their radiographic folder or on the online server (digital).

The patients' ID numbers recording the randomisation method were kept in a separate envelope.

The data was transferred onto a computer database and backed up on Trust-approved encrypted and password protected memory sticks.

The information collected was stored as linked anonymised data.

4.17 Statistical analysis

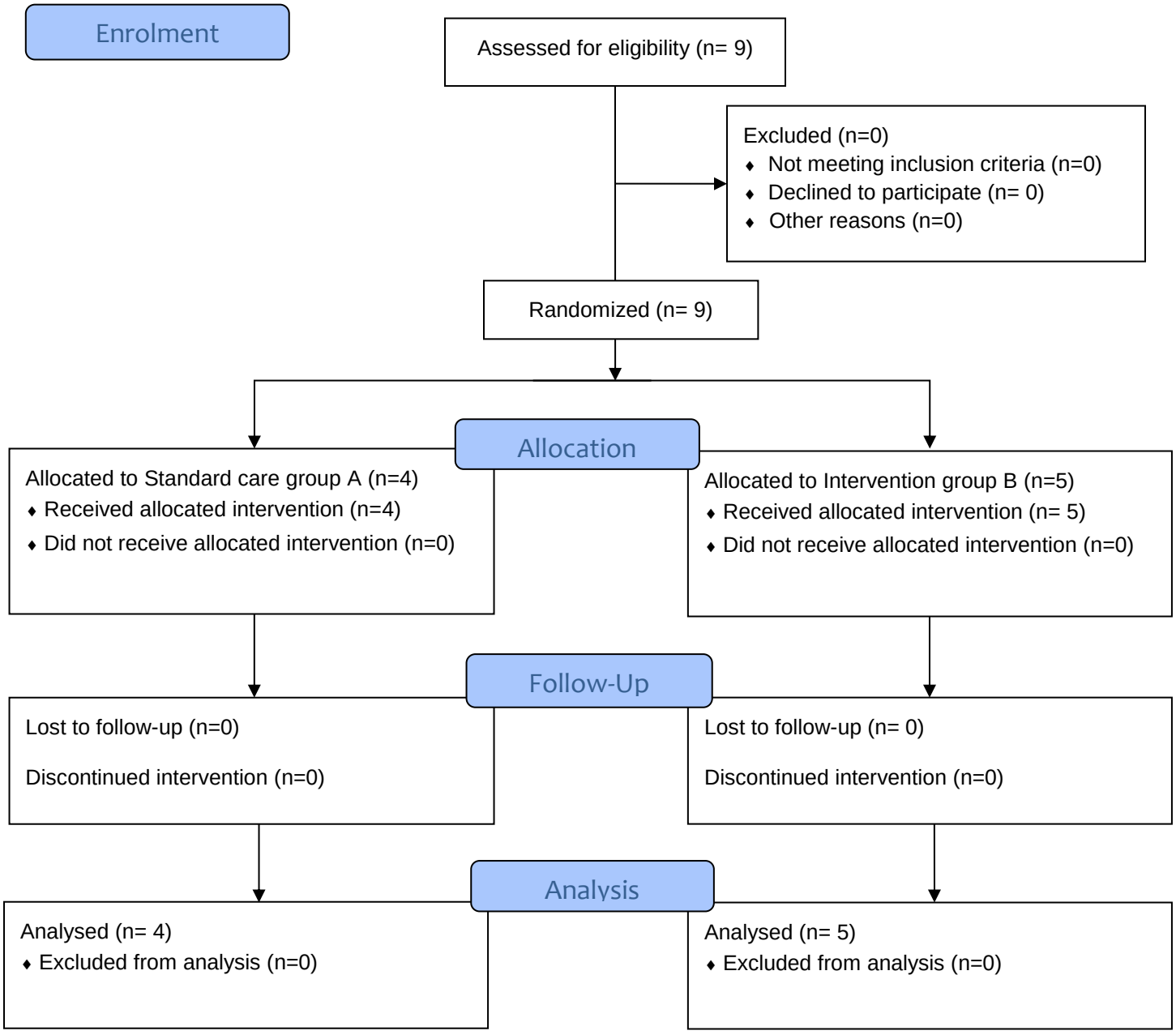
Data was transferred from the data collection forms on a Microsoft© Excel spreadsheet and SPSS© software was used for the statistical analysis.

As a pilot, efficacy testing was not one of the primary aims of this study, as the study was not powered to detect a difference. However, a statistical analysis of the primary outcome data was be carried out, using Fisher's exact test to compare the proportions with retention of the corrected overjet at the end of the study.

The primary outcome was retention of the corrected overjet.

5.0 Results

5.1 Recruitment Flow Diagram



5.2 Interpretation of the flow diagram

During the period of recruitment from 1/10/2012 until 30/4/2013, 9 patients were enrolled into the trial. There was a 3-month follow up of the patients from the date that they entered into it.

From the flow chart it can be seen that 9 patients were suitable for recruitment. They were randomly assigned to each group by the aforementioned randomisation process, involving a statistician who by the use of a computer program generated the allocations. These were then typed onto a card and placed in sequentially numbered opaque envelopes. When a patient was recruited into the trial, the first envelope was then collected.

Four patients were randomly allocated to the Transition Group A (standard care) and five were randomly allocated to the No Transition Group B (intervention). There were no patients declined to participate or dropped out during the study period. All patients were followed up and included in the statistical analysis and examined in original randomly allocated groups.

5.3 Sample Characteristics

	Group A	Group B	Total
N	4	5	9
Gender (%) Male Female	 2 (50) 2 (50)	 1 (20) 4 (80)	 3 (33.33) 6 (66.66)
Mean average overjet in mm (s.d.)	7.1 (0.85)	10.5 (3)	8.8 (2.82)
Pre-treatment overjet (mm) ≥ 15 12-14 10-12 8-10 6-8	 0 0 0 1 3	 1 0 2 1 1	 1 0 2 2 4
IOTN (DHC) *5a* *4a*	 0 4	 3 2	 3 6

Table 1- Sample characteristics

5.3.1 Gender

The recruited sample was primarily female at 66.6% compared to males at 33.3% (table 1). In Group A there was even distribution of males and females (table 1). In Group B, it was predominantly females at 80%.

5.3.2 Pre-treatment overjet

The average overjet in Group A was 7.1 mm and the average overjet in Group B was 10.5mm (table 1).

The majority of the total sample, 8 patients (89%) had an overjet within 6-12 mm. There was only 1 patient (11%) who had an overjet of 15 mm or above.

In Group A all the patients had an overjet within 6-10 mm; where as in Group B 3 patients (60%) had an overjet over 10 mm.

5.3.3 Casuals appointments, Unable to attend (UTA) and failure to attend (FTA) (Secondary outcomes)

Table 2

	Group A	Group B	Total
N	4	5	9
Casuals appointments	2	4	6
Unable to attend (UTA)	0	1	1
Failure to attends (FTA)	1	0	1

Table 2 – secondary outcome results

Casual appointments

In the total sample there were 6 patients who attended an extra casual appointment out with their routine appointment (table 2). The reasons cited for attending these appointments were commonly an orthodontic bracket that had debonded, a piece of wire causing mucosal trauma and the functional appliance not fitting properly.

UTAs

In the total sample only 1 patient cancelled an appointment, this appointment was subsequently rearranged for within 2 weeks of original date (table 1).

FTAs

In the total sample only 1 patient failed to attend an appointment. The patient was then sent out another appointment following the protocol. The patient cited that they forgot about the appointment as the reasons for failing to attend the routine appointment. The patient was accommodated within 2 weeks of original appointment.

5.3.4 IOTN (Brook and Shaw, 1989)

All patients had a Dental Health Component (DHC) of either a 4a or 5a. A 4a is an overjet of 6.1 mm or above but less than 9mm and a 5a is an overjet greater than or equal to 9 mm.

In group A, all patients fell into the 4a category (table 1). In group B, two patients had a 4a and three had a 5a (Table1).

Overall, 33.3% of the sample was a 5a and 66.66% was a 4a.

5.4 Primary outcome data

The primary outcome of the study is the presence or absence of a corrected overjet at the end of the trial.

	Group A	Group B	Total
Successful	2 (50%)	3 (60%)	5 (55.6%)
Unsuccessful	2 (50%)	2 (40%)	4 (44.4%)
Total	4 (100%)	5 (100%)	9 (100%)

Table 3- primary outcome data

The results show that in total from both groups, 5 patients (55.6%) were successful in maintaining the corrected overjet after the functional appliance therapy.

In group A, both the number of patients who succeeded and the number of patients who did not succeed were equal.

In group B, 3 (60%) patients were successful in maintaining the corrected overjet after the functional appliance therapy and 2 (40%) were not successful.

A Fisher's exact test was carried out to compare the proportions with retention of the corrected overjet. The *p* value was 0.643 (Appendix 1) which was substantially higher than the 0.05 level of statistical significance set for this study.

Harms or unintended effects

During this trial there were no harms or unintended effects that could have caused it to be discontinued.

5.5 Comparison of primary outcome data with secondary outcomes

	Group A		Group B	
N	unsuccessful	successful	unsuccessful	successful
Primary outcome (%)	2 (50)	2 (50)	2 (40)	3 (60)
Gender (%) Male Female	 2 (100) 0 (0)	 0 (0) 2 (100)	 0 (0) 2 (100)	 1 (33.33) 2 (66.66)
Mean overjet in mm (s.d.)	7.3 (1.41)	7.0 (0.35)	9.3 (2.47)	11.3 (3.51)
Pre-treatment overjet (mm) ≥ 15 12-14 10-12 8-10 6-8	 0 0 0 0 2	 0 0 0 1 1	 0 0 1 0 1	 1 0 1 1 0
Casuals	1	1	1	3
Unable to attend (UTAs)	0	0	0	1
Failure to attend (FTAs)	0	1	0	0

Table 4-comparison of primary outcome with secondary outcomes

Gender

Females were shown to have a higher success rate than males with four females being successful across both groups compared to one male.

The patients that were successful in Group A were all female and in Group B 2/3 of the successful patients were female. The patients that were unsuccessful in Group A were male and in Group A were female.

Pre-treatment overjet

The average overjet of the successful patients in Group A was 7.3 mm and 7 mm in the unsuccessful patients. The average overjet of the successful patients in Group B was 11.3 mm and 9.3 mm in the unsuccessful patients.

In Group A all the successful patients had an overjet between 6-8 mm and the unsuccessful patients had an overjet between 6-10 mm.

In Group B there was a wider variability of overjet in the successful patients, with overjet values ranging from 8 mm to greater than 15 mm. In the unsuccessful patients in Group B the range was between 6-12 mm.

Casual appointments

In Group A, 1 successful and 1 unsuccessful patient attended the casuals' clinic. In Group B, 3 successful and 1 unsuccessful patients attended the casuals' clinic.

UTAs

One patient in study cancelled an appointment and this was subsequently rearranged. They were a successful patient in Group B.

FTAs

One patient in study failed to attend an appointment and this was subsequently rearranged. They were a successful patient in Group A.

6.0 Discussion

6.1 Introduction

The first recorded Randomised Controlled Trial (RCT) was published only 50 years ago (Medical Research Council, 1948). Pioneered by the statistician Austin Bradford Hill, he managed to persuade a number of doctors to randomly allocate patients with Tuberculosis to either streptomycin or no treatment. It was partly thought up to conserve the small supply of the antibiotic streptomycin and to find out if this line of treatment actually was effective against tuberculosis.

Randomised Controlled Trials are one of the simplest, most powerful and revolutionary tools of research (Jadad and Rennie, 1998; Schlutz *et al*., 1995). An RCT in simple terms is a type of clinical study whereby participants are randomly allocated into groups of several clinical interventions. It can be used to evaluate a therapeutic intervention, whether it is old and never been tested or new and never been clinically evaluated. This then allows comparisons to be made of the differences, if any between the groups studied after the patients receive the intervention. The groups of patients should have similar baseline characteristics, in order for any change between the groups to either be by chance or due to one of the interventions that a particular group received. The gold standard way of allocating these patients to the groups is by random allocation. This means that all the participants have the same chance of entering each of the groups being studied. Therefore allocation is not influenced by the clinicians, researchers or even patient persuasion.

This study was carried out as a pilot or it could be defined as a feasibility study. This type of study is a smaller version of a trial that is designed to test the logistics and gather information prior to a full scale project. A pilot or feasibility study can highlight any potential problems before a larger scale study is set up. They are usually smaller in comparison and they therefore can only provide limited information. This means that a pilot study alone cannot alone provide adequate data on variability for a power analysis to estimate the accurate number of participants needed. This was highlighted in this study, due to the small numbers recruited; an accurate sample size was unable to be calculated.

Although an accurate sample size for future studies was unable to be calculated, the pilot study was invaluable in finding out if this trial was viable. It gave the researcher insight into the workings of a study of this kind and find out if any aspect needed to be improved upon. This study highlighted that this study had no patient recruitment issues and all patients were willing to participate. It also showed that the clinicians complied with data collection and no patients had to be excluded due to incomplete data. However, a few difficulties were highlighted including getting sufficient patient numbers and getting all of the clinicians in the department to participate. These will be discussed at length.

Reporting of an RCT can be varied and the published results may be a short tailed version of the information required to fully interpret the results. In 1996, an international group of clinical epidemiologists, biostatisticians, and journal editors published a statement called CONSORT (Consolidation of the Standards of Reporting Trials) (Begg *et al*, 1996). The aim of this statement was to improve the standards of written reports of RCTs and to ensure that the readers find all

the information that they require to interpret the results correctly and with confidence. This statement included a checklist of 21 items and a flow diagram that should be adopted by authors to show the flow of the participants through the study from the start of the recruitment to the conclusion of the study. There was an update to this in 2010 (Schultz *et al,* 2010) and they also produced a 25 point checklist for reporting of a RCT. It provides the researcher teams a framework to avoid omitting important information at the point of producing the final report. It also an aid of producing a clear and adept report that allows the reader ease of digesting all of the information.

6.2Results

In total 9 patients were analysed for the trial.

6.2.1Gender

From Table 1 it can be seen that the recruited sample is primarily female at 66.6% compared to males at 33.3%. Females were shown to have a higher success rate than males with four females being successful across both groups compared to one male (table 4). These results were not tested for significance due to the small sample size.

The results were similar to other studies which have shown that females have a greater uptake to orthodontics than male patients (Banks *et al*, 1988; Roberts *et al*, 1989). This could be related to more female patients presenting themselves for and seeking out treatment in comparison to their male counterparts. Table 4 illustrates the success rate for both Group A and Group B, and it can be seen that patients that were successful in group A were all female and for group B two

thirds of the successful patients were female. Conversely, it showed that all the males in Group A were unsuccessful and the unsuccessful patients in Group B were female.

6.2.2 Pre-treatment overjet

In table 4 the average pre-treatment overjet for Group A and Group B has been summarised. In Group A the average overjet was 7.1 mm and this is further broken down into the successful and unsuccessful patients. The average overjet of the successful patients was 7.3 mm and 7 mm for the unsuccessful patients.

The average overjet in Group B was 10.5 mm. The average overjet of the successful patients was 11.3 mm and 9.3 mm for the unsuccessful patients.

These results may suggest that there may be an association with increased overjet and compliance, with the patients who present with a larger pre-treatment overjet being more likely to be successful with treatment. Further investigation of this would be needed to confirm this statistically. A possible explanation could be that patients with a very large overjet may be more aesthetically aware of the position of the prominent teeth and then will be more likely to comply with treatment. Whereas patients who have a smaller overjet may have less of a cosmetic concern and therefore have less motivation to wear the functional appliance. A functional appliance often affects a patient's speech and mastication at the beginning of treatment and can be very uncomfortable to wear.

In Table 1, the pre-treatment overjet in relation to the total sample was summarised. The majority of the total sample, 8 patients (89%) had an overjet within 6-12 mm. There was only 1 patient (11%) who had an overjet of 15 mm or above.

In Group A all the patients had an overjet within 6-10 mm; where as in Group B, 3 patients (60%) had an overjet over 10 mm.

It was perhaps unsurprising to find most patients presenting with average increased overjet between 6-12 mm and only one patient with a 15 mm overjet. No patients had an overjet less than 6 mm, this was to be expected as patients who were in need of the proposed treatment.

When looking at the total sample, it appears that Group B distribution of overjet was skewed in favour of patients who started with a higher pre-treatment overjet. This was evident as in Group A all the patients had an overjet within 6-10 mm, in contrast to Group B, where 3 patients (60%) had an overjet over 10 mm. As this was only a small sample, it is difficult to draw any firm conclusions on this and it may not have been the case if a larger sample was achieved allowing both groups to have a more even distribution. If future studies were to be carried out it may be something that should be stratified for when carrying out the randomisation process to ensure that there is a similar range of overjet presents in each group. This would lead to an increase in sample size needed in an already limited population of patients that would be suitable for inclusion to the trial.

The overjet characteristics of Group A displayed in table 4, show the number of successful and unsuccessful patients in relation to their pre-treatment overjet. In Group A all the successful patients had an overjet between 6-8 mm and the unsuccessful patients had an overjet between 6-10 mm. This could suggest that in Group A that both the successful and unsuccessful patients had a similar overjet and it was not a factor in success. Although due to the small sample size, firm conclusions cannot be drawn on this.

In contrast to Group A, table 4 also shows the number of successful and not successful patients in Group B in relation to their pre-treatment overjet. In group B, the successful patients appeared to have a higher pre-treatment overjet than the unsuccessful patients. As discussed earlier this could be due to the patients who had a larger pre-treatment overjet were more inclined to comply with treatment.

6.2.3 Casuals appointments, Unable to attend (UTAs) and failure to attend (FTAs)

Casual appointments

It can be seen from table 2, that in the total sample there were 6 patients who attended an extra casual appointment out with their routine appointment. The reasons cited for attending these appointments were commonly an orthodontic bracket that had debonded a piece of wire causing buccal trauma and the appliance 'not fitting properly'.

In Group A, 1 successful and 1 unsuccessful patient attended the casual clinic. In Group B, 3 successful and 1 unsuccessful patients attended the casuals' clinic (table 4).

More patients who were in Group B attended casual appointment compared to Group A which could be explained by the method of transition. Group B had no transition and therefore treatment continued straight into fixed appliances which was perhaps unfamiliar to them. The fixed appliances differ greatly from the functional appliance that the patient had previous worn and was familiar with, they cannot be removed and they are attached directly to each individual tooth with a bracket. A wire is then attached to this bracket with an elastomeric module, this interaction with the bracket and wire causes the tooth movement. As the appliance is bonded directly on to the tooth it can be debonded if the patient does not adhere to the dietary

instructions. One of the other reasons cited for attending the casual appointment was that the wire was digging into the buccal mucosa causing trauma. This is a very common presentation in the casual clinic as even the smallest protruding piece of wire can cause the patient discomfort. Therefore it could be hypothesised that because the fixed appliance was new to the patient and differed from previous appliance that they would have been more likely to attend the casuals clinic that a patient in group A who had the same familiar appliance to them.

6.2.4 UTAs and FTAs

From table 2 it can be seen that in the total sample only 1 patient cancelled an appointment, this appointment was subsequently rearranged for within 2 weeks of original date. The one patient who cancelled the appointment was from Group B and did not affect the treatment outcome as they were successful at retaining their overjet.

Table 2 highlighted that in the total sample only 1 patient failed to attend an appointment. The patient was then sent out another appointment following the protocol. The patient cited that they 'forgot about the appointment' as the reasons for failing to attend. The patient was accommodated within 2 weeks of original appointment.

These very low rates of UTAs and FTAs could be explained by the patients being motivated and enthusiastic enough to want to participate in the clinical trial. This has been previously described in the medical and dental literature as the Hawthorne effect. As it has never really been proven, it cannot be measured or accounted. The expectation that has been previously put forward by researchers is that a well-designed RCT with a control group should suffer the Hawthorne effect (Mayo, 1949) equally in the intervention and control groups and effectively cancel itself out.

6.3 IOTN

The Index of Treatment Need (IOTN) was developed in the UK in 1989 (Brook and Shaw, 1989), where the majority of the orthodontic patients have been treated under the National Health Service (NHS) since 1948. As with any publicly-funded limited resource system, this epidemiological tool has been converted into a method of prioritising treatment provision in the primary care sector.

It was based on the Swedish National board for Welfare Index developed by Linder-Aronson (1974). It defined the need for treatment in both terms of the dental health benefit and aesthetic handicapping.

The index is divided into two components, the Dental Health Component (DHC) and the Aesthetic Component (AC). The DHC is comprised five categories of increasing treatment need of severity of malocclusion, from Grade 1 (no need) to Grade 5 (great need) for treatment. There are a number of different features of malocclusion that are scored, these features are Missing teeth, Overjet, Crossbites, Displacement of contact points (crowding) and Overbite. The DHC is hierarchical and for each individual patient the highest score is found and recorded, irrespective of any other features on the list that the patient may have. The grades one to five are further sub divided using letters which correspond to the feature of the malocclusion that has been scored.

The AC is based on a series of ten photographs, which show a gradual worsening of dental aesthetics. The patient is then given a score from one to ten based on the perceived aesthetic impairment of the individual malocclusion, not the morphological similarities. Only the patient's frontal dental view is analysed and the rest of the aesthetics of the face and smile are not taken

into account, which could be a limitation of the aesthetic component. It is also very subjective as different clinicians may perceive different malocclusion traits as worse than others and that would mean that patients may score differently between clinicians, another shortfall of this component.

Table 1 displays the IOTN of the sample. All patients in the study had a DHC of either a 4a or 5a. A 4a is an overjet of 6.1 mm or above but less than 9 mm and a 5a is an overjet greater than or equal to 9 mm.

In group A, all patients fell into the 4a category. In group B, two patients were a 4a and three 5a.

This small sample is representative of what could be expected to see in patients in the Hospital service functional appliance treatment list. It again reinforced the findings that the patients in Group B had a larger pre-treatment overjet than Group A, as 3 patients had an overjet greater than 9 mm (5a). There were no patients in Group A that fitted into the 5a category.

6.4 Primary outcome data

The primary outcome of the study was the presence or absence of a corrected overjet at the end of the study within 2 mm of the overjet at the end of functional appliance therapy.

From the results in table 3, it can be seen that in total in both groups, 5 patients (55.6%) were successful in maintaining the corrected overjet after the Twin Block therapy.

In Group A, both the number of patients who succeeded and the number of patients who were unsuccessful equal.

In Group B, 3 (60%) patients were successful in maintaining the corrected overjet after the Twin-block therapy and 2 (40%) patients were unsuccessful.

A Fisher's exact test was carried out to compare the proportions with retention of the corrected overjet. The *p* value was 0.643 (Appendix 1) which was substantially higher than the 0.05 level of statistical significance set for this study.

Due to the small sample size, the study was not powered to detect the clinical significance difference between the groups and therefore it was not possible to determine if the intervention is better at maintaining the control group than the standard care group.

This pilot did not give sufficient information to accurately estimate the proportion of successful retention of the overjet in the transition group. If a new study was designed to detect a minimum clinically difference of 20 percentage points (40% success in transition group vs. 60% in no transition group), a sample size of 97 patients per group would be required to detect the difference with 80% power at the 5% significant level. This is the highest sample size that would be required for a difference of 20 percentage points. If a more accurate estimate of the proportion in the transition group was available, this required sample size may reduce.

Due to logistical difficulties of recruiting 97 patients per group, there may be a need to alter the clinical and statistical parameters of a future study. This could help reduce the patient numbers, albeit diminish the usefulness of the clinical data. These could be:

1. Increase the cut off point for determining success or failure. The cut-off point in this project was set to 2 mm; this could be increased to 3 or 4 mm instead. The foreseeable

issue with increasing this figure would be that there some of the cases would be partially treated and therefore in contradiction to the inclusion criteria as set in the beginning of the study.

2. Recruit from multiple treatment centres. A larger number of treatment centres would reduce the average number of patients per centre, which could be easier to recruit. This would be implementable in a health service with unlimited funds; in the current economic climate it may be difficult to justify the resources that would be required to undertake this.
3. Reducing the clinical significance to less than 20% difference between intervention and control groups. However, this would make the results much less meaningful to use in clinical practice.

6.5 Limitations

There are a number of limitations with this study and they are mostly due to the small number of patients that were able to be recruited. As there were only a small number of results that were able to be analysed it does not lead to any substantial conclusions. It was also impossible to carry out an accurate estimation of a sample size needed to carry out a full scale trial. From our small sample, an imprecise calculation was carried out but this suggests that a large, possibly un-obtainable sample of 97 patients per group was needed. This large number needed may indicate to that there may be no differences between the two types of intervention.

6.6 Recruitment

The process and problems of recruiting patients for a Randomised Controlled Trial have been widely published in the medical literature (Treweek *et al*., 2010). It is very important for an RCT to recruit the sample size that has been deemed needed by statistical analysis. If this desired number of patients is not recruited the study may be underpowered, this may potentially lead to the reporting of clinically important effects as non-significant (Fletcher *et al*., 2012). If these findings are accepted as not significant, then potentially effective interventions may be abandoned or a delayed until other sufficiently powered trials is carried out. It is also important that the sample size calculations are carried out prospectively in order to make sure that the correct numbers of patients are recruited in order to have sufficient power to detect a statistically significant difference if there is one. Ultimately the success of this type of study depends on patient participation.

In the medical literature it has been widely reported that there is poor uptake in recruitment in RCTs. There are a number of published studies that highlight how common it is to have problems with recruitment in relation to studies involving healthcare. It has been reported that 50% of healthcare RCT's fail to recruit to their target sample size (Fletcher *et al*., 2012). Multiple studies have indicated that recruitment is very poor; Rafferty *et al* (2008) found that two thirds of funded Trials failed to pass their recruitment target. Toreien *et al* (2009) also echoed this in their review of all RCT's published in July –December 2004, they found that of 133 Trials, 21% that reported sample size calculations failed to achieve adequate numbers at randomisation and 48% at outcome assessment. Studies by McDonald *et al* (2006) and Bower *et al* (2003) highlighted the problem of recruitment within a specified timescale. Bower suggested that less than a third of

primary care trials in the UK recruited the patients in the original timescale; both studies suggested that there is a barrier to recruitment for RCTs.

A Cochrane review carried out by the Treweek *et al* (2010) wanted to quantify strategies that improve patient participation in RCTs. They investigated randomised and quasi-randomised trials that looked at ways of increasing patient recruitment. This Cochrane review found that patient recruitment increased when non-responders were contacted by telephone. It was also found that using an 'opt-out' clause rather than 'opt-in' can increase patient recruitment or an open design to allow patients know which allocation they are going to be receiving. These potential recommendations unfortunately have their disadvantages as if it is an open trial; it is there by definition un-blinded. This would introduce an element of bias, which then reduces the clinical value of the RCT findings by introducing unspecified confounding factors.

There are a number of barriers to patient participation that have been cited in the literature that patients have indicated. Patients often feel that there may be additional demands on them if they enter a trial and it may be simpler not to participate. To try and overcome this drawback, all trials should be made as simple and least disrupting as possible for patients in order to improve recruitment. Patients may be concerned of additional financial aspects in that there may be additional costs if they take part as well as additional visits are needed. Although not deemed to be of significance in this study and therefore not implemented, travel costs have been previously reimbursed to encourage subjects to participate. In addition, of concern might be about treatment preference and as the 'control' group may provide unfavourable treatment outcomes. Their concerns were alleviated at the outset of this study and all discussions were clear and

transparent. The advantages and disadvantages of treatment options and the unknown significance of the two were discussed at length and the patients were invited to ask questions to clarify any aspects of treatment.

Furthermore, the rationale for the trial was used in order to educate the patients on aim of the study. The patient documentation was also made to be 'patient friendly' as in the literature this has been found to have a profound effect on patient recruitment (Penn and Steer, 1990). There was very few technical terms used and most were expressed in layman's terms. An example of using layman's terms was the technical term 'overjet' was replaced with 'the gap between the top and bottom front teeth'.

One of the other barriers to patient recruitment to a RCT is the recruiting clinician. This area has not been thoroughly investigated to find out if there are any interventions that improve clinician recruitment. This is one of the most important factors as a patient cannot recruit themselves and therefore a clinician needs to be motivated and interested to recruit patients and maintain this level of enthusiasm throughout the recruitment period. A Cochrane review carried out by Rendell *et al* (2007) aimed to assess the evidence for the effect of disincentives and incentives on the extent to which clinicians invite eligible patients to participate in RCTs of healthcare interventions. They were unable to include any RCTs and there was insufficient data for a full assessment of quality. Eleven observational studies were eventually included in this review. The review found that clinicians who agreed to participate because they were acquainted with the researchers were less likely to participate than those otherwise motivated (1 study, 2 sided p=0.04 Fisher's exact test) and (Odds Ratio [OR] 0.4, 95% confidence interval [CI] 0.2-0.9, 1 study).

It also found that clinicians who had recruited were more likely to report some difficulties including 'trials involve extra work' (OR 92.94, 95% CI 4.54-1902.11; $p \leq 0.01$, 1 study) and 'inviting patients to participate is embarrassing' (Chi square 15.55, df -1, p ≤0.0001, 1 study). The effect of the need to discuss clinical uncertainty was unclear but concern that the doctor - patient relationship would be adversely affected by participation was a deterrent (chi square -7.25, df -1, p=0.007, I study). Extra caution was taken to ensure that no patients were discouraged from participating in the study from the author's point of view.

It has also been found that there is a wide disparity between the number of clinicians who agree in principal to recruit their own patients into the trial and the number who actually actively recruit patients. A study by Taylor, (1994, 1995) suggested that in the year following completion of a survey on trials, only 35% of clinicians who had agreed to take part had recruited any patients. This study suggested possible reasons for this, a possible explanation being that when considering recruitment of a particular patient the disincentives becomes more salient, the incentives less attractive and or additional disincentives are encountered or anticipated. In another study by Benson *et al* (1991), it was cited that 73% of clinicians agreed with the statement that 'excessive time is required for patient follow up on a study' but surprisingly only 26% stated this as the reason for not entering patients into RCTs.

The recruitment process was one of the more challenging aspects of the trial. I personally encountered many of the barriers that I have previously discussed, suggesting that it they don't only apply to the medical field but also to the dental field. It is a wide spread problem in clinical RCTs in all domains of healthcare where patient and clinician recruitment is needed.

It was very difficult to get the large number of patients needed in order to get results of any significance, as only a small number of the patients who enter our department each year are suitable for inclusion into the trial. This with the added difficulty of time constraints meant that the window of opportunity for recruitment of patients was very small. In retrospect, the recruitment period would have been better to have been longer in order to include as many patients as possible and thus increase the sample size.

It was very difficult to try and recruit some of the Consultants to allow their patients to be included in the trial as they were initially sceptical. Their main objection was that they felt that they managed the transition effectively and efficiently, and through their own experiences had now felt that they had a clinical practice that suited them. The inclusion of the standard care Group A to have any form of transition was to ensure that the RCT was not restricting their clinical freedom completely. This alleviated the scepticism of some of the clinicians. In the end, all of the Consultants agreed to participate in the study and allow their patients to be recruited but as found in the literature only a small number of the Consultants actually recruited any of their patients into the clinical trial.

The patients and parents were all willing to participate, there was no patient that declined to enter the study or removed themselves from it. It was designed in order to be as patient friendly as possible in order to make sure that they did not have to give up additional time to attend extra appointments in order to encourage them to enter the trial. As discussed earlier it is important to try to recruit as many patients as possible to ensure that the study has enough participants to allow any conclusions to be drawn.

6.7 Data collection

During the course of this project, all the information that was needed was available. The clinicians who were taking the clinical measurements followed the protocol and there were no patients that had to be excluded due to poor data collection.

The data that was to be collected was clinical measurements that have to been taken at every routine visit and this may explain why there was such excellent compliance within recording of the data. It caused no additional clinical time or appointments to be needed over and above the routine visits. A data collection form was designed in order for data collection and dissemination of the results to be efficient and easily blinded to ensure that the patient's allocation remained unknown. It allowed the form to be separate from the rest of the patient's clinical notes and to be stored securely.

6.8 Generalisability

Unfortunately due to the very small sample size, it has not been possible to make any general statements about the results or to bring them into the context of the clinical environment. The only part of the study that can be effectively compared is the way the trial was carried out. It was run in a fairly standardised way and it could have been comparable to the real life clinical environment .The results could have been applied if there were indeed any differences found in the two interventions that were tested.

6.9 Bias

At present an RCT is the most efficient and ethical way of assessing clinical interventions. But it does not mean that they are free from all the pitfalls of other types of trial design. They can be flawed and have bias introduced into them. This will be discussed in this section.

In the lay literature, bias has been defined as "opinion or feeling that strongly favours one side of an argument or one item in a group or series; predisposition; prejudice (Hornby, 4th edition). In research related to healthcare, it is defined as any factor or process that deviates the results or conclusions of a trial systematically away from the truth (Anderson, 1990; Owen, 1982; Sackett, 1979). This deviation away from the truth can cause results of a RCT to be overestimated or underestimated. Although it can be present in the control or intervention group it commonly leads to an exaggeration of the effects of the intervention being studied.

Bias can be introduced voluntarily; however it is more likely to be introduced involuntarily. It can occur anywhere, from the planning at the very beginning, outcome measurements, analysis of the data, interpretation of the results, and the publication of the results (Sackett, 1979). Studies have shown that bias can occur even in the reading of trials.

One of the single most important factors of an RCT is the potential to minimise or eliminate the effect of selection bias. When carried out correctly, randomisation can keep the groups as similar as possible to start with so that any differences that occur can be contributed to the interventions being investigated. No other form of study design has the ability to balance the known and unknown confounding factors between the groups. It is of the upmost importance that we aim to try to reduce the potential influence of bias in clinical studies, as the results of RCTs on a

sample population can then be inferred onto a wider population. If bias is not reduced then there is often a systematic deviation from the true value, often an over estimation of the effect of the intervention is seen.

Randomisation ensures that all participants have the same chance of being selected for either intervention without being influenced by the clinician, researcher or the participant. There are a number of different methods for allocation of participants. A number of the methods that are described in the production of the final report are often misleadingly described a random allocation, when in fact they are not. A few examples of this type of 'pseudo-random' or 'quasi-random' are allocation by date of birth, hospital number or date that they are invited to participate in the study. These methods do not give each patient an equal chance to enter a study; therefore it is not random allocation. Often these methods can be easily worked out and it is easy to find out which group each patient is randomly allocated to and this knowledge can affect recruitment of the patients into the trial. It may influence a clinician whether or not to enter a patient into the study as they could work out which treatment group they would be allocated too. This could affect the results and introduce bias (Altman, 1971; Schlutz *et al*., 1995).

Theoretically, by allocation of the patients by random sequence, the baseline characteristics are balanced at baseline. By keeping the groups as similar as possible at the start of the study, the investigators will be more likely to isolate and quantify the impact that the intervention has on the participants and that the other factors will have minimal interference as they are present across the whole sample.

There are a number of ways that can be utilised to generate a random sequence of allocation. There are two golden rules that should be followed when setting up a random sequence generator regardless of which method itself. The allocation must be defined prior to starting, for example prior to flipping a coin there must be an allocation for what heads or tails stands for. The other important factor is that this must be continued throughout the whole of the trial. The most simple of methods to generate a sequence if there are only two groups is flipping a coin or rolling a die. There are more complex methods involving random number tables or computer generated sequences.

The actual method selected is chosen by investigators, the numbers of patients allocated to each group will differ at any given time point. To minimise these differences, stratified or block randomisation can be carried out. Stratification is used to try and keep all the number of participants receiving each allocation as similar as possible. It is also used to keep the characteristics of the participants similar over the groups. The researcher must identify a factor or factors that are known to be related to the outcome of the study. Once the factor or factors have been identified then a separate block randomisation is carried out for each factor to ensure that the groups are balanced within each stratum.

Bias also occurs when RCTs are being disseminated. The main source of this bias comes from during this period of the RCT timeline are, publication bias, country of publication bias, time lag bias, and potential breakthrough bias. Publication bias has been investigated and it has been shown that results that give a trial a positive response are more favourably published than results that show a negative response or no difference (Dickersin, 1990; Duley and Farrell; Rennie and

Flanagin, 1992). The only way to reduce this publication bias is to ensure that all RCTs are registered with a general body and that all results are recorded even if the results are not favourable. The system needs to be transparent but this is an area of great debate and this contentious issue will go on and on. Language bias is similar to publication bias, in that positive results are more likely to be published in English (Egger *et al*., 1997). Country of publication bias is when a particular country tends to only publish the results of positive studies. One of the big sources of bias during dissemination of reports is time lag bias. This is where the time taken to publish the results differs depending on the results of the trial (Ioannidis, 1991; Jadad and Rennie, 1998; Vickers *et al*., 1998). It seems that positive results tend to be published quicker than their negative counterparts. Potential breakthrough bias is something is becoming more widespread in the lay literature. This type involves partial utilisation of a study's results by the media in order to labour a reportable point. The accuracy of the statements that stem from the studies is, often, poor. Unfortunately, this type of bias has a large impact factor as the public tend to fail to understand that these results are often very misleading and full of bias.

As this project is in the process being written up, the World Medical Association has updated the Helsinki Declaration. The 2013 version also discusses issues related to dissemination of health research information. That includes making sure that RCTs are registered in publicly accessible databases and that those databases include not positive results but also negative or inconclusive. This will hopefully bring to the fore front the importance of having all of the information available and allowing everyone to have the freedom to fully appreciate all the results.

In order to reduce the potential biases discussed, a number of features were incorporated into the design of the RCT. To eliminate selection bias, the patients were randomised by a computer generated sequence by a statistician. To reduce allocation bias, the allocation of the groups was concealed using opaque envelopes. This was carried out by people unrelated to the project and therefore the researchers and the clinicians recruiting the patients were also unaware of the sequence. The envelopes were stored in a locked drawer until a patient was recruited and the clinician was then handed an envelope from a sequential order. This was then opened with the patient in the Orthodontic Clinic.

For this study, blocked randomisation was used which is a technique used to ensure that the number of participants assigned to each group is equal. The process of blocked randomisation is set up in blocks of a pre-determined size. The block size must be blinded from the investigator performing the study and, if the study is non-blinded, the block sizes should vary randomly (otherwise the last allocation(s) in a block would, in effect, be unconcealed). This has to be unknown to the investigator or it is possible to work out the sequence and therefore induce a form of selection bias.

The randomisation process was stratified by consultant. The process of stratifying the randomisation is the technique for ensuring that an important baseline variable which could be a potential confounding factor is more evenly distributed between the two groups than if left to chance. It was decided to stratify by Consultant as it was felt that this could be an important baseline factor as different clinicians may carry out the transition from functional appliance to fixed appliances in a dissimilar manner. Each consultant was given the clinical freedom to choose

which form of transition was chosen for a patient if they were in the standard care group. Therefore by being given this clinical freedom there had the potential for a number of different forms of transition.

Unfortunately, this study is open to ascertainment bias, which is when the results or conclusions are systematically distorted by knowledge of which intervention the patient is receiving. This bias can be introduced by the patient, the clinician carrying out the treatment and the investigator assessing or analysing the outcomes. Ideally, the best way to reduce this type of bias is to keep the people involved in the study unaware of the identity for as long as possible.

Ascertainment bias can be minimised in two points in the timeline of an RCT. It can be minimised when the data is being actively collated and when the data is being analysed. As with all clinical RCTs it is often not possible to blind the clinician carrying out the procedure and the patient. In this case, it was not possible to blind the clinician as they would have to know what group they had in order to carry out the prescribed treatment. The patient would also know which group that they were allocated to. They would either be told that their functional appliance is being discontinued and they were proceeding into fixed appliance therapy or that they were keeping their functional appliance for a little longer. The only form of blinding that was able to be carried out was by the investigator, who could look at the collated data and carry out analysis without knowing which group had the intervention form of treatment.

Bias can affect any part of a trial from beginning to end and it comes from all different sources. Hopefully, as illustrated above this study was as robust as possible, given its limitations and the

author was acutely aware of different types of bias and tried to ensure that they were addressed accordingly.

6.10 Sample size

When carrying out an RCT, an important part of the study is ensuring that the correct sample size is present in order to detect a clinically significant difference, if there is indeed one. Often it can be the case when a small trial shows that there is no statistically significant effect; it is assumed that there is no treatment effect at all. It could however be that the trial was not large enough to produce a significant effect. If this is the case then it has been said it should be thought of as 'no evidence of benefit' rather than 'evidence of no benefit'. This makes a huge difference on how the area of interest is perceived as if there has been a small or badly designed study that shows 'no evidence of benefit', and then it would be more likely to be re-investigated with improvements.

Achieving the desired sample size as discussed early can be challenging. If there is a large disparity between the desired sample size and the actual sample size, it is better to carry out a small randomised study. However, these studies have to be thought of as hypothesis forming rather than hypothesis testing.

In this case I carried out a feasibility study with one of the aims of the trial being to try predicting a sample size for a future study. Unfortunately, due to the small sample size achieved, this pilot did not give sufficient information to accurately estimate the proportion of successful retention of overjet in the transition group. If a new study was designed to detect a minimum clinically difference of 20 percentage points (40% success in transition group vs. 60% in no transition

group), a sample size of 97 patients per group would be required to detect the difference with 80% power at the 0.05 significant level. This is the highest sample size that would be required for a difference of 20 percentage points. As mentioned previously, if a more accurate estimate of the proportion in the transition group was available, this required sample size may reduce.

Having a sample size of 97 patients per group would not make this project suitable to be carried out in a single unit orthodontic department. The large sample size would make fulfilment of the required sample be almost impossible to obtain unless it was carried out over a number of years. This is because as a single department will only have around 40-50 patients suitable for functional appliance therapy per year if all patients are available for recruitment.

Ideally, this study would be suitable to be carried out as a Multi-Centre Randomised Control Trial and this would allow a larger sample size to be easily obtained. But this does not come without its difficulties. Having a study of this size would need multi centres being used for recruitment and this would have to be closely monitored to ensure that the standard protocol is adhered to and that all other procedures are being followed. It would also need a central area to which the data could be stored and where the allocations were kept. A trial of this scale would also be within multiple clinical sites and therefore need the approval of all involved and also the close working of all the clinical staff over the centres. There would be a larger financial implication in comparison to only having one unit where no further costs are incurred, as you may need to employ someone who is not directly involved with the study to carry out the administrative duties that would be needed in order to make sure it runs efficiently and is closely monitored.

6.11 Ethical approval and NHS research and development

When deciding to plan a clinical trial involving patients it must go through rigorous approval as otherwise to ensure that the experimentation planned was not unwillingly harming the subjects by withholding a highly efficient treatment or asking a question previously answered in the literature. To have an effective project, the clinician must have true equipoise in the different arms of treatment being investigated. It would be thought of as un-ethical to recruit patients into a group that could cause them a detrimental effect to their health. But if the clinician has genuine uncertainty of the outcome for a patient then it becomes ethical to randomise the patient and in their best interest.

As this project involved patient recruitment, it had to be sent for ethical approval prior to commencement of the trial. The ethics committees have a number of both clinical and lay members, and are guided by the declaration of Helsinki. The Declaration of Helsinki was set up in 1964 by the World Medical Association and the most recent update being October 2013 to ensure that it remains up-to-date and accommodates advances in the medical and ethical fields. It was developed as a statement of ethical principles for medical research involving human subjects. It includes principles on safe guarding research subjects, informed consent, minimising risk to the subject and adhering to an approved research protocol. The declaration is considered a fundamental document in the ethics of healthcare research. As a result of this the principles have been taken up by UK and international guidelines and regulations. The 2013 version also discusses issues related to dissemination of health research information. That includes making sure that RCTs are registered in publicly accessible databases and that those databases include not only positive results but also findings that are negative or inconclusive.

Applying for ethical approval to the novice researcher is a learning curve in itself. This project had to be sent to the local REC committee that dealt with children as our participants would be less than 16 years old. The ethical approval processes are set up primarily to deal with medical research involving studies of new drugs or new surgical techniques and hence rigorous investigation of these applications is needed prior to being approved for patient recruitment.

However, as a dental based project as part of a doctoral degree this proved one of the most challenging aspect of the whole research experience. Even though the project was not introducing any new techniques but comparing different clinical effectively methods, the project still had to go through the same intense investigation as trialling a new drug. The ethics committees are primarily made up of clinicians and researchers with a medical background and therefore have a limited understanding of the dental projects. This can make the process even more difficult when the committees have no background or understanding of the project and it can cause delays while trying to explain about the project and the dental speciality. This research was carried out as part of a doctoral research within a fixed term speciality training appointment; timing was of critical importance in order to complete the study within the time frame. As this was a pilot study, this first experience of an application for ethics and this has provided an excellent insight into how the ethical approval process works. For future research it will hopefully ensure that the process is far more effective and efficient on the researcher's behalf.

In addition, the project have to be approved ethically it had to be approved by the NHS Research and Development department as it was being carried out by NHS funding. This proved to be time consuming and like ethical approval, it could be difficult to navigate through the process at times.

The project was initially approved to be carried out a 3 hospital sites within the deanery but all within different hospital trusts. This meant that the NHS Research and Development had to be approved separately for each NHS trust. This again was time restricting and also meant that some trusts responded quicker than other which meant that you could not proceed at the same rate with all departments. They also had to make sure that they were happy with the accompanying information leaflets, consent forms even though they were approved through the ethics process. Fortunately all NHS trusts were happy with all of the information leaflets and had no changes to be made other than their trust logo.

The recurring theme throughout the ethical approval and NHS research and Development process was that it was very time consuming and it required a lot of planning and organisation. This was just as an important learning experience as the results of this project. Without having been through the processes, the researcher will not gain the experience and skills to carry with them for future research projects. It would also allow them to make the process more efficient and ensure that the project is commenced at a faster pace.

If the whole process was to be repeated as part of a fixed term training contract, it would be recommended that gaining the ethical approval should be the first priority. This is the time consuming step and restricts the flow of the project and can have the project stagnating at one point with nothing else to do but wait.

7.0 Conclusions

1. The null hypothesis could not be rejected based on the results of this study. Therefore, there is no evidence of a difference in using any form of transition following successful completion of functional appliance therapy compared to no transition.

2. A secondary objective of this study was to investigate the size of sample size needed to appropriately power a Trial of this type. This was measured to 97 patients per group with α set at 80% and significance level of 0.05.

3. Due to the small sample size, the study is not powered to detect a clinical significance difference between the groups and therefore it is not possible to determine if the intervention is better at maintaining the control group than the standard care group

4. This pilot did not give sufficient information to accurately estimate the proportion of successful retention of the overjet in the transition group.

8.0 Future Research

This pilot study was carried out in order to assess the feasibility of this Trial and to establish if any difficulties in recruitment, data collection and analysis of the data. It was used to perform sample size calculations in order to assess if a project of this type was of benefit to be carried out in a larger scale.

The study could also be extended to follow the patients throughout treatment until completion of active orthodontic treatment, the treatment mechanics could then be looked at; to investigate if there were any differences between the two groups. Alternatively, the total length of treatment, the final overjet, PAR score and extraction rate could be assessed.

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World Medical Association Declaration of Helsinki (1964)

10.0 Appendices

10.1 Assent form

Version 1.1

Centre Number:
Study Number:
Patient Identification Number for this trial:

ASSENT FORM

Title of Project: A single-blind prospective pilot Randomised Control Trial (RCT) to investigate the need for a transition phase following successful completion of functional appliance therapy

Name of Researcher: Joanna Thomson

Please initial box

1. I confirm that I have read and understand the information sheet dated August 2012 (version 1.1) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that the data collected during the study will be analysed by the study investigators. I give permission for these individuals to have access to my records. ☐

4. I agree to take part in the above study. ☐

_____	_____	_____
Participant	Date	Signature

_____	_____	_____

10.2 Patient Consent form

Informed Consent Form for _____.

This informed consent form is for the parents of children between the ages of 10 and 15 years who attend clinic Liverpool University Dental Hospital for orthodontic treatment. We are asking those children who have had a take-in/take-out block brace to participate in our study (known as a single blinded randomized clinical trial) which will investigate the need for and the management of a waiting period before the fixed brace is put on.

Miss Joanna Thomson

Liverpool University

This Informed Consent Form has two parts:

- **Information Sheet (to share information about the study with you)**
- **Certificate of Consent (for signatures if you agree that your child may participate)**

You will be given a copy of the full Informed Consent Form

PART I: Information Sheet

Introduction

I am Joanna Thomson, an orthodontic trainee at Liverpool University Dental Hospital. As part of my training, I am studying the need for a waiting time between your child's take-in/take-out removable brace and the fitting of a fixed brace.

I explain what is involved and invite you to allow your child to take part in this research. You do not have to decide today whether or not you are willing for your child to participate, and you can let us know when you have taken a decision either way.

There may be some words that you do not understand. If so, please stop me as we go through the information together and I will explain more fully. If you then have any other questions, either myself or any other member of the orthodontic staff will be pleased to answer them.

Purpose

The purpose of this trial is to find out if we need to wait a while between removing the take-in/take-out block brace and putting the fixed brace on your child's teeth. At present there is no evidence to suggest whether there is any advantage to this**.**

Type of Research Intervention

One group (the control group) will undergo a waiting time, the length of which is chosen by the clinician, before the fixed braces are fitted. The other group (the intervention group) will have the fixed appliances (fixed braces) put on immediately after the first brace/s have been taken off.

Participant selection

We are inviting your child to take part in the study as he/she is first of all undergoing what is known as functional appliance therapy before a second phase of treatment with fixed appliances.

Voluntary Participation

Your decision to allow your child to participate in this study is entirely voluntary. Should you initially agree but later change your mind, your child will cease to take part in the study. This will not affect his or her treatment in the orthodontic department here in any way.

Procedures

All the methods used in this trial are routinely used in the transition phase. As we are unsure as to whether any particular method is better than another, we need compare the results. This involves putting the participating patients into randomly assigned groups.

Your child will undergo routine orthodontic treatment and on all visits standard clinical measurements will be taken.

Duration

Your child will take part in the research project for three months and attend monthly for the usual routine appointments.

Risks

There are no additional risks attached to participating in this trial beyond routine orthodontic treatment.

Discomfort

There are no additional discomfort from taking part in this trial.

Confidentiality

All information collected from this research project will remain strictly confidential and any information concerning your child will be stored and available to the researchers only. Your child will be identified by a number only and no names will be used. Identity is thus fully protected and will not be shared with anyone.

Sharing the results

The results of this study will be shared with you before being made more widely available. Confidential information and identity will not be revealed at any stage. The results will be published subsequently so that other interested clinicians may benefit from our research.

Right to Refuse or Withdraw

You do not have to agree to your child taking part in this research if you do not wish to do so. By **refusing to allow your child to participate, your treatment or your child's treatment in this department will not be affected in any way**. All treatment will be carried out as initially planned. You may stop your child from participating in the study at any time if you so wish, without either you or your child losing any of your rights as a patient here.

Alternatives to participating

If you do not wish your child to take part in the research, your child will still be provided with the appropriate treatment within the department.

Who to Contact

You may ask questions at any time, before and during the study. If you wish to make any enquiry subsequently, you may contact:

Miss Joanna Thomson

Orthodontic Department,

Liverpool University Dental Hospital,

Pembroke Place,

Liverpool

joannat@liverpool.ac.uk

If you feel that you have not been satisfactorily treated and wish to make a complaint, please contact the following:

Heather Rogers

Research Governance Manager

Research Development & Innovation Dept.

4th Floor Linda McCartney Centre

Royal Liverpool & Broadgreen University Hospital Trust

Prescot Street

Liverpool

L7 8XP

PART II: Certificate of Consent

CERTIFICATE OF CONSENT

I have been invited to allow my child to participate in this research.

I have read the information provided, or it has been read to me.

I have been given the opportunity to ask questions and been satisfied with the answers.

I voluntarily consent for my child to take part in this study.

Print Name of Participant _____

Print Name of Parent or Guardian _____

Signature of Parent or Guardian _____

Date _____/_____/_____

day month year

Statement by the Researcher/Person taking consent

I have accurately read out the information sheet to the parent of the potential participant, and to the best of my ability made sure that the person understands that the following will be done:

1.

2.

3.

I confirm that the parent was given an opportunity to ask questions about the study, and that all the questions asked have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and that the consent has been given freely and voluntarily.

A copy of this ICF has been given to the participant.

Print Name of Researcher/Person taking the consent _____

Signature of Researcher /Person taking the consent _____

Date _____/_____/_____

day month year

10.3 Patient Information Sheet for under-16-year old patients

A single-blind prospective Randomised Control Trial (RCT) to investigate the need for a transition phase following successful completion of functional appliance therapy

INFORMATION SHEET FOR CHILDREN UNDER 16

We are asking you to help us in our research project. Before you decide whether or not to take part, it is important that you understand what the project is about.

Why are we doing this project?

After you have finished wearing your twin-block brace to reduce the gap between your two top front and bottom front teeth, we put fixed braces on which you can't take off. We do not want the gap to come back between wearing the two different sorts of braces, so we have several ways of stopping this happening. In this project we want to try and see which one works best.

Why ask for your help?

We need healthy young people to take part who have a large gap between their top front teeth and also between their bottom front teeth, and who are wearing a twin-block brace as part of their orthodontic treatment.

Do you have to take part?

No, you can choose to not take part.

What will happen if you take part?

We will take certain measurements of your teeth, as we do each time you attend the hospital for your appointments.

How long will the project last?

We will take these measurements of your teeth over 3 months, along with the other usual details that are part of your dental records.

What if I am not happy or have a problem?

You can stop taking part in this project at any time. Your brace treatment will continue as normal.

If you have any questions, feel free to ask and I will be happy to answer them.

Thank you for taking time to read this

10.4 Data Collection Sheet

Name

DOB

RQ No.

DATE	OVERJET	OVERBITE	MOLAR RELATIONSHIP	CANINE RELATIONSHIP	CENTRE LINES	ORAL HYGIENE

10.5 CONSORT Guidelines

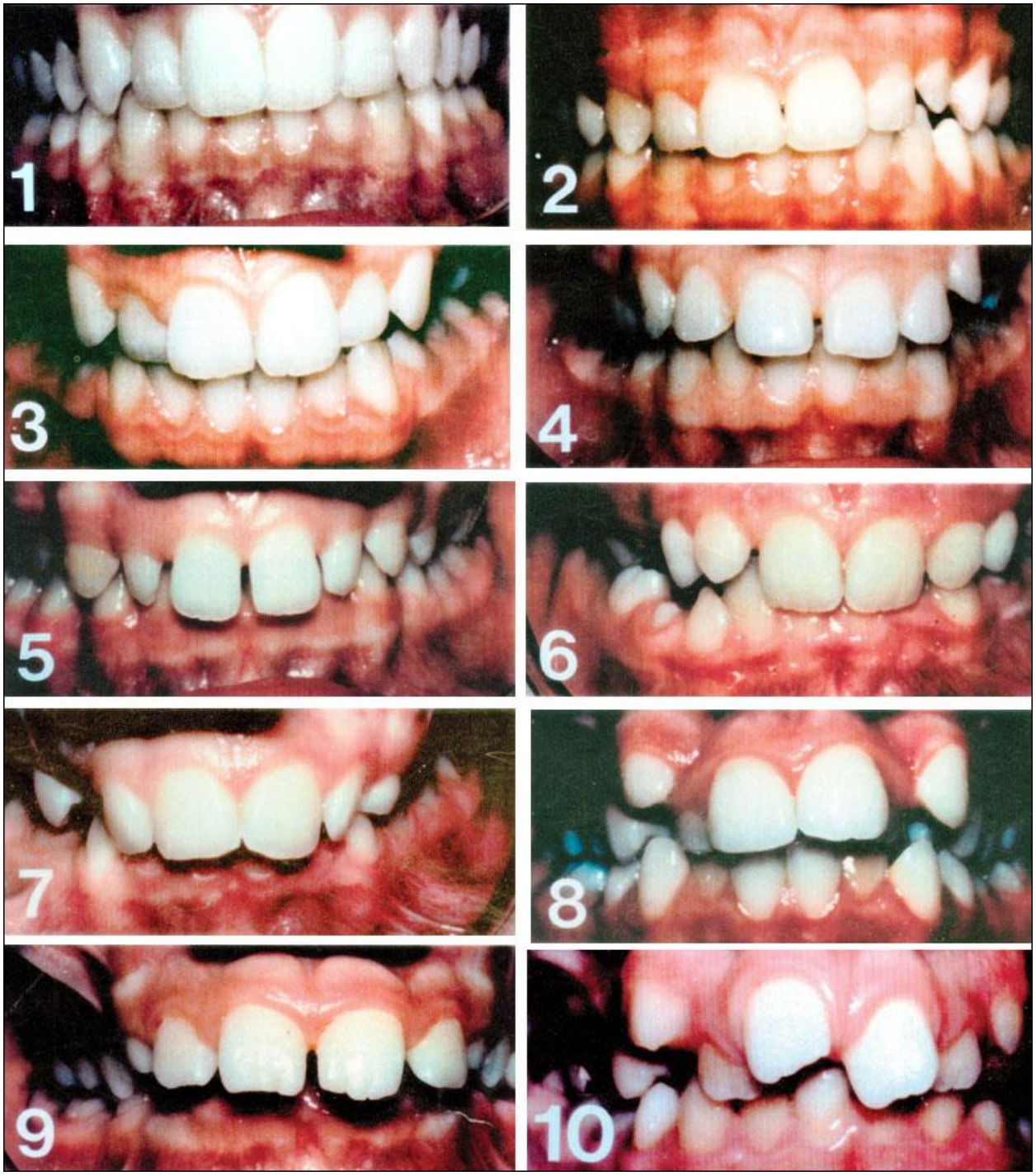
CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic		Checklist item
	1a	Identification as a randomised trial in the title
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)
Background and objectives	2a	Scientific background and explanation of rationale
	2b	Specific objectives or hypotheses
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons
Participants	4a	Eligibility criteria for participants
	4b	Settings and locations where the data were collected
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed
	6b	Any changes to trial outcomes after the trial commenced, with reasons
Sample size	7a	How sample size was determined
	7b	When applicable, explanation of any interim analyses and stopping guidelines
Randomisation:		
Sequence generation	8a	Method used to generate the random allocation sequence
	8b	Type of randomisation; details of any restriction (such as blocking and block size)
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence, describing any steps taken to conceal the sequence until interventions were assigned
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how
	11b	If relevant, description of the similarity of interventions
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses
	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome

Participant flow (a diagram is strongly recommended)	13b	For each group, losses and exclusions after randomisation, together with reasons
Recruitment	14a	Dates defining the periods of recruitment and follow-up
	14b	Why the trial ended or was stopped
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses
Generalisability	21	Generalisability (external validity, applicability) of the trial findings
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence
Other information		
Registration	23	Registration number and name of trial registry
Protocol	24	Where the full trial protocol can be accessed, if available
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org

10.6 IOTN Aesthetic Component



10.7 IOTN Clinical Component

GRADE 5 (Need treatment)	
5.i	Impeded eruption of teeth (except for third molars) due to crowding, displacement, the prescence of supernumerary teeth, retained deciduous teeth and any pathological cause.
5.h	Extensive hypodontia with restorative implications (more than 1 tooth missing in any quadrant) requiring pre-restorative orthodontics.
5.a	Increased overjet greater than 9 mm.
5.m	Reverse overjet greater than 3·5 mm with reported masticatory and speech difficulties.
5.p	Defects of cleft lip and palate and other craniofacial anomalies.
5.s	Submerged deciduous teeth.

GRADE 4 (Need treatment)	
4.h	Less extensive hypodontia requiring prerestorative orthodontics or orthodontic space closure to obviate the need for a prosthesis.
4.a	Increased overjet greater than 6 mm but less than or equal to 9 mm.
4.b	Reverse overjet greater than 3·5 mm with no masticatory or speech difficulties.
4.m	Reverse overjet greater than 1 mm but less than 3·5 mm with recorded masticatory and speech difficulties.
4.c	Anterior or posterior crossbites with greater than 2 mm discrepancy between retruded contact position and intercuspal position.
4.l	Posterior lingual crossbite with no functional occlusal contact in one or both buccal segments.
4.d	Severe contact point displacements greater than 4 mm.
4.e	Extreme lateral or anterior open bites greater than 4 mm.
4.f	Increased and complete overbite with gingival or palatal trauma.
4.t	Partially erupted teeth, tipped and impacted against adjacent teeth.
4.x	Prescence of supernumerary teeth.

GRADE 3 (Borderline need)	
3.a	Increased overjet greater than 3·5 mm but less than or equal to 6 mm with incompetent lips.
3.b	Reverse overjet greater than 1 mm but less than or equal to 3·5 mm.
3.c	Anterior or posterior crossbites with greater than 1 mm but less than or equal to 2 mm discrepancy between retruded contact position and intercuspal position.
3.d	Contact point displacements greater than 2 mm but less than or equal to 4 mm.
3.e	Lateral or anterior open bite greater than 2 mm but less than or equal to 4 mm.
3.f	Deep overbite complete on gingival or palatal tissues but no trauma.

GRADE 2 (Little)	
2.a	Increased overjet greater than 3·5 mm but less than or equal to 6 mm with competent lips.
2.b	Reverse overjet greater than 0 mm but less than or equal to 1 mm.
2.c	Anterior or posterior crossbite with less than or equal to 1 mm discrepancy between retruded contact position and intercuspal position.
2.d	Contact point displacements greater than 1 mm but less than or equal to 2 mm.
2.e	Anterior or posterior openbite greater than 1 mm but less than or equal to 2 mm.
2.f	Increased overbite greater than or equal to 3·5 mm without gingival contact.
2.g	Pre-normal or post-normal occlusions with no other anomalies (includes up to half a unit discrepancy).

GRADE 2 (Little)	
1.	Extremely minor malocclusions including contact point displacements less than 1 mm.